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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,650	03/19/2004	Michael Borns	25436/2382	9645

27495 7590 03/04/2008

AGILENT TECHOLOGIES INC
P.O BOX 7599
BLDG E , LEGAL
LOVELAND, CO 80537-0599

EXAMINER
STAPLES, MARK

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
03/04/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com
maria_carroll@non.agilent.com
laurie_schutze@agilent.com

Office Action Summary	Application No.	Applicant(s)	
	10/805,650	BORNS, MICHAEL	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/17/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-18,21-29 and 31-46* is/are pending in the application.

4a) Of the above claim(s) *12, 14, 16-18, 21-24, and 31-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,15,25-29 and 40-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/17/2007 has been entered.

2. Applicant's amendment of claims 28, 29, and 41 in the paper filed on 10/17/2007 and presented in the paper filed 12/17/2007 is acknowledged. Applicant's cancellation of claims 11, 19, 20, and 30 and submission of new claims 42-46 in the paper filed on 12/17/2007 is acknowledged. The submission of a declaration under 37 C.F.R. § 1.132 in the paper filed on 12/17/2007 is acknowledged.

Claims 1-10, 13, 15, 25-29, and 40-46 are pending and at issue.

Applicant's arguments filed on 12/17/2007 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objection and Rejections that are Moot / Withdrawn

Specification

3. The objection to the trademark DEEP VENT® is withdrawn. As applicant correctly points out, this trademark is adequately identified by a trademark symbol.

Cancelled Claims

4. The rejections of cancelled claims 11, 19, 20, and 30 are moot and therefore are withdrawn.

Declaration under 37 C.F.R. § 1.132

5. The declaration under 37 CFR 1.132 filed on 12/17/2007 is insufficient to overcome the rejection of claims 1-10, 12-18, 21-29, and 31-46 based upon Wang (2001) as set forth in the last Office action because the declaration: (1) provides evidence only showing that a non-chimeric polymerase which is *PFU Turbo* loses activity above pH 8.8 (see Attachment B), whereas Wang teaches a chimeric polymerase which is a DNA polymerase fusion which functions at pH 9 (see Wang p. 40, line 14); (2) does not provide evidence that a sole chimeric polymerase which is a DNA polymerase fusion as claimed (that is, not a blend) functions at pH 9.3 to pH of 14 as claimed; and (3) thus does not provide evidence supporting an argument that it would have been a surprising discovery to one of ordinary skill in the art that a sole DNA polymerase fusion, as claimed, has enhanced PCR performance efficiency above pH 9.

Rejections that are Maintained

Claim Rejections Maintained - 35 USC § 112 First Paragraph

6. The rejection of claims 1-10, 13, 15, 25-29, and 40 under 35 U.S.C. 112, first paragraph, is maintained because the specification, while being enabling for a range of pH 9.3 to 10, does not reasonably provide enablement for a range of pH 9.3 to 14. Applicant's arguments filed 12/17/2007 have been fully considered but they are not persuasive.

Applicant argues that the Office has not met the initial burden to establish a reasonable basis to question the enablement of the claimed invention. Examiner disagrees as the hydrolysis of protein at pH 10 and higher, as taught by Ernster (1985) more than meets this initial burden. Furthermore, as known by one of ordinary skill in the art and conveyed by Ernster (see column 6 lines 19-23) as the pH increases, protein hydrolysis increases. Thus a working example of a protein at pH 10.0 provides no evidence of that protein working at higher pH, especially in the range of pH 12-14 where Applicant has no working examples. Also, the increase in pH is not a linear increase but a log increase (pH being the negative log of hydrogen ion concentration) so that pH 12 is a hundred fold more alkaline than pH 10, while pH 14 at the extreme of alkalinity is a hundred fold more alkaline than pH 12. Thus as the claims recite a range of pH 9.3 to 14, the rejection is maintained.

Claim Rejections Maintained - 35 USC § 103

7. The rejection of claims 1-4, 7-11, 13, 15, 19, 25-30, and 40 under 35 U.S.C. 103(a) as being unpatentable over Wang (2001) is maintained. Applicant's arguments filed 12/17/2007 have been fully considered but they are not persuasive.

Applicant argues that that one of ordinary skill in the art would not optimize a pH range in view of Wang, as Wang teaches: (1) a pH of 8.8 which is removed from pH 9.3 and (2) a commercial buffer which Applicant asserts one of ordinary skill in the art would assume to be optimized. However, it is the entire teachings of Wang which were used in the claim rejections and not just these two elements. Wang teaches not only pH 8.8 but pH 9.0 as well (see p. 40, line 14). Thus as Wang teaches different alkaline pH's are useful for DNA polymerases, it would have been obvious to optimize pH. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use a pH of 9.3 and above as used by the applicant or in the range of ph 9.0 as used by Wang since these differences in pH would not be expected to greatly alter the conditions for amplification. One of ordinary skill in the art would have not expected that the activity of a DNA polymerase fusion would vanish at pH 9.3 when it was fully functional at pH 9.0. This is consistent with the Federal Circuit decision in In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003) "We have also held that a prima facie case of obviousness exists when the claimed range and the prior art range do not overlap but are close enough such that one skilled in the art would have expected them to have the same properties." Thus, an ordinary practitioner would have

recognized that the droplet size could be adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of pH 9.3 was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art of pH 9.0. As noted, a skilled artisan would expect a pH of 9.0 to have nearly identical properties in the amplification of nucleic acids. Thus, an ordinary practitioner would have recognized that the results could be adjusted to maximize the desired results.

Applicant further argues that the declaration of Michael Borns supports the unobviousness of a range of pH 9.3 to 14. However the declaration is not sufficient to overcome the rejection (see section 5 above). The argument regarding the wild type polymerase is also addressed there.

Applicant also argues that that there is no specific teaching, suggestion, or motivation in Wang to vary the pH. Examiner disagrees as Wang does vary the pH, using both pH 8.8 and pH 9.0 which suggest that a DNA polymerase fusion would have activity at other pH's. Regardless, the argument that a specific teaching, suggestion, or motivation is required to support an obviousness rejection over prior art is foreclosed by *KSR* (see the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, Bd. Pat.

App. & Interf. June 25, 2007 which cites *KSR*, 82 USPQ2d at 1396, available at http://www.uspto.gov.web/offices/dcom/bpai/prec/fd071925.pdf). One could have arrived at the claimed invention by routine optimization as noted above.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "blends comprising DNA polymerases" show enhanced activity) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus the rejection is maintained.

8. The rejection of claims 5 and 6 under 35 U.S.C. 103(a) as being unpatentable over Wang (2001) and further in view of Sanger et al. (1977) is maintained. Applicant's arguments filed 12/17/2007 have been fully considered but they are not persuasive.

Applicant argues that as the rejection of base claims under Wang should be withdrawn, so too should this rejection be withdrawn. However, the base claims remain rejected under Wang and therefore this rejection is maintained as well.

New Rejections

New Claim Rejections - 35 USC § 112, First Paragraph

9. Claims 1-10, 13, 15, 25-29, and 40-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed methods recite one polymerase, a DNA polymerase fusion comprising wild type *Pyrococcus furiosus* polymerase I fused to *Sulfolobus solfataricus* SSso7d protein, and at the same time the claimed methods omit the essential element of the disclosed invention which is a blend of both a chimeric DNA polymerase fusion and a non-chimeric polymerase. See instant Figures 1-4 and the description of the blends used there on pages 28-30. And in lines 11-15 on p. 1, the instant specification discloses:

> "The present invention relates to blends of chimeric and non chimeric DNA polymerases, methods for their synthesis, and methods for their use. The DNA polymerase blends disclosed herein are useful for many recombinant DNA techniques, especially nucleic acid sequencing, nucleic acid amplification by the polymerase chain reaction (PCR) or mutagenesis."

The specification provides no support for use of one DNA polymerase fusion at pH 9.3 to 14 as claimed.

New Claim Rejections - 35 USC § 112, Second Paragraph

10. Claims 1-10, 13, 15, 25-29, and 40-46 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 1-10, 12-18, 21-29, and 31-46 omit the essential element of the declared invention, which is blends of polymerases, can be found in the reply filed 12/17/2007, Declaration under 37 C.F.R. § 1.132. In that paper, applicant has stated that the Applicant was surprised to discover that increasing the pH above 9 enhances, rather than impairs, PCR efficiency of DNA polymerase fusions (plural) and blends comprising the same (see p. 5 item 18). This statement indicates that the invention is different from what is defined in the claim(s) because the claims are methods reciting one polymerase, a single DNA polymerase fusion comprising wild type *Pyrococcus furiosus* polymerase I fused to *Sulfolobus solfataricus* SSso7d protein.

New Rejections

New Claim Rejections - 35 USC § 103

11. Claims 41-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang as applied to claims 1, 3, 5, 7, and 9 above.

Wang teaches as noted above and in Office Actions mailed on 08/17/2007 and 12/08/2006.

Regarding claim 41, Wang teaches where the activity is extension time in PCR (see for example p. 8, lines 4-6).

Regarding claims 42-46, Wang teaches using a DNA polymerase fusion at both pH 8.8 (see p. 29, line 14) and pH 9.0 (see p. 40, line 14). Thus as Wang teaches different alkaline pH's are useful for DNA polymerases, it would have been obvious to optimize pH. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the claimed pH of 9.5 and above as used by the applicant or in the range of pH 9.0 as used by Wang since these differences in pH would not be expected to greatly alter the conditions for amplification. One of ordinary skill in the art would have not expected that the activity of a DNA polymerase fusion would vanish at pH 9.3 when it was fully functional at pH 9.0. This is consistent with the Federal Circuit decision in In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003) "We have also held that a prima facie case of obviousness exists when the claimed range and the prior art range do not overlap but are close enough such that one skilled in the art would have expected them to have the same properties." Thus, an ordinary practitioner would have recognized that the droplet size could be adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> "More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Routine optimization is not considered inventive and no evidence has been presented that the selection of pH 9.3 was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art of pH 9.0. As noted, a skilled artisan would expect a pH of 9.0 to have nearly identical properties in the amplification of nucleic acids. Thus, an ordinary practitioner would have recognized that the results could be adjusted to maximize the desired results.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
/M. S./
Examiner, Art Unit 1637
February 22, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637